

REMARKS**1. Status of Case**

Applicant appreciates the Examiner's acknowledgement of Applicant's timely filing of a Response to an Office Action on July 10, 2009.

2. Status of Claims

Applicant appreciates the Examiner's acknowledgement that claims 18-31 and 33 are pending and that claims 18-29 have been examined. Applicant also appreciates the Examiner's acknowledgement that claims 30-31 and 33 have been withdrawn as being drawn to a non-elected invention and that Applicant timely traversed the restriction requirement in its reply filed on February 16, 2007.

3-4. Rejection of Claims 18-29 under 35 U.S.C. 112, second paragraph

The Examiner has rejected claims 18-29 under 35 U.S.C. 112, first paragraph for the reasons of record.

Specifically, the Examiner contends that claims 18-29 are indefinite over the recitation of, "said aneuploidy being determined by an unequal binding." With that said, solely for the sake of advancing prosecution, and without prejudice or disclaimer of the subject matter therein, claim 18 has been amended to remove the term, "said aneuploidy being determined by an unequal binding" and has replaced it with the phrase, "wherein the presence of an aneuploidy is determined by a difference in the detectable signal emitted by said sample or said standard bound to said binding agent" to assist in clarifying this aspect of the present invention.

The Examiner also contends that claims 27-29 are indefinite over the recitation of "said binding agent comprises a nucleic acid immobilized on a microparticle." Solely for the sake of advancing prosecution, and without prejudice or disclaimer of the subject matter therein,

Applicant has amended claim 18 in several ways (see enclosed Preliminary Amendment) to assist in clarifying this aspect of the invention, as well.

Additionally, the Examiner contends that claims 18-29 are indefinite over the recitation of, "binding of said sample and said sample to said binding agent." Solely for the sake of advancing prosecution, and without prejudice or disclaimer of the subject matter therein, claim 18 has been amended to remove the term, "binding of said sample and said sample to said binding agent" and has replaced it with the phrase, "wherein the presence of an aneuploidy is determined by a difference in the detectable signal emitted by said sample or said standard bound to said binding agent" to assist in clarifying this aspect of the present invention.

In light of the foregoing, Applicant respectfully requests withdrawal of the rejection of claims 18-29 under 35 U.S.C. 112, first paragraph.

5. Rejection of Claims 18-21, 23, 24 and 26-28 under 35 U.S.C. 103(a)

The Examiner has rejected claims 18-21, 23-24 and 26-28 under 35 U.S.C. 103(a) as being unpatentable over Pinkel (U.S. Patent No. 6,562,565) ("Pinkel") in view of Mohammed (PGPUB 2003/0124584) ("Mohammed") and further in view of Singh et al. (WO 02/40698) ("Singh") for the reasons of record.

Applicant respectfully asserts that there are key distinctions between the present invention and the methods of Pinkel. One such distinction is that the microparticles of the present invention can be identified individually from one another. This is possible because they may be internally or externally labeled with a reporter molecule, such as a fluorescent marker, and/or by utilizing a variety of microparticle sizes (1 to 10 μm). Exemplary methods for labeling the microparticles are described on page 23 of the specification. Labeling the microparticles of the present invention allows for identification of individual microparticles via distinct emission of a specific fluorescence spectrum. Utilizing microparticles labeled with distinct reporter molecules and of a variety of sizes allows for simultaneous separation of microparticles by both fluorescence and size, such as by FACS analysis. This ability to utilize fluorescently labeled

microparticles of different sizes results in a distinct multiplex platform where both samples and standards can hybridize to complementary nucleic acid sequences on microparticles allowing for differences in hybridization to be identified with a high-degree of sensitivity and specificity.

In contrast to the present invention, Pinkel describes the use of, "target elements" that include beads and target nucleic acids. In the methods of Pinkel, the sequences of interest in both samples and standards are linked to different fluorescent molecules that are able to hybridize to the nucleic acid portion of the target elements. In contrast to the methods of the present invention, the target elements of Pinkel themselves are not fluorescent and the beads cannot be distinguished by size. Additionally, Pinkel discloses the use of FISH and/or fluorescence microscopy that cannot provide the degree of specificity regarding the sequence to which a sample or standard has hybridized when multiple target nucleic acid sequences are analyzed in a single reaction. The methods of Pinkel are only capable of showing the comparative fluorescence between the sample and/or standard that has hybridized to the nucleic acid array.

As can be seen from the remarks above, the methods of the present invention provide significant advances in microparticle multiplex technology. The methods allow for specific polynucleotide sequences, complementary to the fluorescent standard or fluorescent sample, to be bound to a specific microparticle that can be defined by size, fluorescent label and fluorescent intensity. (See for example, Table 3 of the specification) The methods also allow for variation in the relative intensity of the emission spectra of a hybridized sample compared to a hybridized standard to be identified. The microparticles involved in differential hybridization can also correspond to a specific nucleic acid sequence. These characteristics of the microparticles allow for the determination of the existence and location of aneuploidy in a chromosome of a subject.

Solely for the sake of advancing prosecution, and without prejudice or disclaimer of the subject matter therein, claim 18 has been amended to assist in clarifying the above-referenced aspects of the present invention.

As previously asserted by Applicant, in order for an Examiner to establish a *prima facie* case of obviousness, the Examiner must show that each and every one of the claim limitations was suggested or taught by the prior art being relied upon. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Additionally, “[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art.” *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Applicant respectfully asserts that this burden has not been met as there are many aspects of the present invention that Pinkel does not teach. Additionally, Applicant respectfully asserts that the aforementioned deficiencies were not taught or suggested by Mohammed or Singh even in view of Ibanez.

In light of the above arguments, Applicant respectfully requests withdrawal of the rejections of record of claims 18-21, 23-24 and 26-28 under 35 U.S.C. 103(a).

Concluding Remarks

In view of the foregoing, Applicant respectfully submits that the rejections have been overcome and respectfully requests that the rejections be removed and the claims placed in condition for allowance. In the event the Examiner has any questions regarding the Applicant's position, a telephone call to the undersigned representative is requested.

Respectfully Submitted,

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Date



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